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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/066,255    04/24/98    BUECHLER

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EXAMINER
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HM12/0725

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ART UNIT	PAPER NUMBER

1627

16

DATE MAILED:

07/25/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Advisory Action

Application No.

09/066,255

Applicant(s)

Buechler et al

Examiner

Maurie E. Garcia, Ph. D.

Art Unit

1627



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Jul 9, 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

### THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires THREE months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on Jul 9, 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);
  - (b) ☐ they raise the issue of new matter. (See NOTE below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE:

4. ☐ Applicant's reply has overcome the following rejection(s):  
\_\_\_\_\_
5. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in separate, timely filed amendment cancelling the non-allowable claim(s).
6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
Please see attached.
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):  
Claim(s) allowed: \_\_\_\_\_  
Claim(s) objected to: \_\_\_\_\_  
Claim(s) rejected: 28, 30, 32, and 34
9. ☐ The proposed drawing correction filed on \_\_\_\_\_ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
11. ☐ Other: \_\_\_\_\_

PADMASHRI PONNALURI  
PRIMARY EXAMINER

### **ADVISORY ACTION**

#### *Attachment*

1. Applicant's arguments filed July 9, 2001 have been fully considered but they are not found persuasive and the rejection of claims 28, 30, 32 and 34 is maintained. The arguments are addressed in detail below.
2. Concerning the rejection under 35 USC 112, second paragraph: Applicant argues that "ligand analogue" is definite (Response, pages 2-3). However, the examiner maintains that this term makes it impossible to determine the metes and bounds of the invention. It is not clear what are the similarities and differences between the ligand and the ligand analogue; that is, how "analogous" must these two compounds be? The terminology (coupled with the instant specification) simply does not provide a standard for ascertaining the requisite degree of "analogy" applicant intends.
3. Concerning the rejections under 35 USC 103: Applicant argues that there is no motivation to combine (Response, page 4, top and elsewhere). In response to these arguments, it is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the

art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). As stated in the previous action, the examiner's position is that the *combined* teachings of the references render applicant's invention prima facie obvious to one of ordinary skill. This is elaborated upon below.

4. As stated in the previous action, the Margaron et al reference teaches compounds that have superior absorption properties. See Margaron et al (page 188):

"[b]ecause of the perturbation of the (na)phthalocyanine D<sub>4h</sub> symmetry and the modification of the acenallation, the degree of the sulfonation of the different condensation products can readily be deduced from the electronic spectra which shift from maxima around 680-720 nm, in the case of the trisulfonated M-NSB<sub>3</sub>P, to major absorption bands between 720-770 nm, in the case of monosulfonated M-N<sub>3</sub>SBP."

Thus, this shift in absorption maxima is what is being referred to by the examiner as superior since the reference teaches absorption above 680 nm is preferred (see page 188, top, of the reference).

5. Margaron et al also teach that their phthalocyanine derivatives are useful because they "can readily absorb light toward the red end of the physical spectrum". Consider the following from Margaron et al (page 187 bottom through page 188, top):

"The rationale for the latter [molecules that absorb more strongly towards the red end of the spectrum] is that light above 680 nm allows for deeper penetration into biological tissues *as well as the availability of less expensive and more reliable light sources at these higher wavelengths*" (emphasis added)

Thus, Margaron et al teach an advantage for absorbing toward the red end of the spectrum as one could use less expensive and more reliable light sources for such wavelengths. Thus, the use of

the phthalocyanine derivatives of Margaron et al as labels in a conjugate (as taught by Renzoni et al) would be obvious to make use of such advantages.

6. Note, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). In the instant case, the beneficial result of the combination of references is being able to use “a less expensive and more reliable light source” and also compounds that have superior absorption properties as taught by Margaron et al.

7. Applicant argues that “nothing of record discloses or suggests that molecules useful in cancer phototherapy would be useful as labels in assay methods” (Response, page 5, 1<sup>st</sup> paragraph). The examiner respectfully disagrees. Renzoni et al teaches phthalocyanine reagents/derivatives “useful as *fluorescent reporting groups*, imaging agents and also as *therapeutic agents*” (emphasis added; see column 1, lines 17-25 of the patent). Specifically, the phthalocyanines of Renzoni are conjugated to biologically active agents such as antibodies (column 39, lines 1-25), peptides or nucleotides (see claim 3 of the reference) and can be used in biological assays (see Example 16, column 39). The reference clearly teaches phthalocyanines can also be used in photodynamic therapy (see Example 15, column 38).

8. Applicant again argues concerning the fluorescence properties of the instant “hybrid phthalocyanine derivative[s]” with respect to the teachings of the reference, stating again that there is no motivation to combine (Response, pages 6-7 and elsewhere). However the examiner maintains that it would have been *prima facie* obvious to one of ordinary skill in the art to use the hybrid phthalocyanine derivatives of Margaron et al as a label in the conjugates of Renzoni et al for the advantages set forth *supra*.

9. As stated previously, the fluorescence properties of the instant “hybrid phthalocyanine derivative[s]” are ***not being claimed***. There is nothing in the instant claims with respect to a specific stokes shift and/or intensity or any other particulars of the fluorescence of the molecule. In fact, there is nothing in the instant claims that limits them to fluorescence at all. The claims merely state “generating a detectable signal”.

10. Also as stated previously, the compounds of the Margaron et al reference meet **all** of the limitations of the “water-soluble hybrid phthalocyanine derivatives” of the claims and thus would have the same properties of such compounds. Fluorescence is a property that depends on the physical structure of a compound and thus would be an intrinsic property of the molecule itself. Also, it is well known in the art that phthalocyanine derivatives are fluorescent, see teachings of Renzoni et al for example. Renzoni et al teach the use of water-soluble phthalocyanine derivatives as fluorescent labels in conjugates. The examiner recognizes that the phthalocyanine derivatives of Renzoni et al are not “hybrid phthalocyanine derivatives” as

instantly defined; however, they possess a *high degree of structural similarity* to those claimed. It would have been obvious to substitute one structurally similar fluorescent label for the other, especially considering the teachings of Margaron et al concerning the advantageous properties of their phthalocyanine derivative compounds.

11. Applicant again refers to the “advantageously large stokes shifts of the water-soluble hybrid phthalocyanine derivatives of the instantly claimed methods” (Response, page 8, top) and discusses the data provided in Table 2 of the instant specification. While it is noted that data regarding the Stokes shifts of several compounds is indeed provided in this Table, there is no *comparison* provided with respect to the performance of these compounds with other “hybrid phthalocyanine derivatives”. Moreover, the compounds in Table 2 of the specification are not specifically claimed. Additionally, as stated above, the fluorescence properties of the instant “hybrid phthalocyanine derivative[s]” are also not being claimed. Again, the compounds of Margaron et al meet **all** of the limitations of the “water-soluble hybrid phthalocyanine derivatives” of the claims and thus would have the *same properties* of such compounds. Lastly, any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (In MPEP § 716.02).

12. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Response, page 7, bottom), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The examiner maintains that the combined teachings of the cited references indicate information that was within the level of ordinary skill and render the claimed invention prima facie obvious.

13. Finally, with respect to the statement in the rejection concerning the Renzoni reference (Response, page 4, 3<sup>rd</sup> paragraph), the examiner respectfully believes that this was taken out of context. The statement the rejection is as follows:

“However, use of phthalocyanine derivatives in conjugates was well known in the art at the time of filing. Renzoni et al teach water-soluble phthalocyanine derivatives (see column 3, lines 29-55) that read directly on those of the instant claims.”

So the part of the Renzoni reference that “reads on” the instant invention is the water-soluble phthalocyanine derivatives taught thereby. As stated in the previous action, the examiner recognizes that the phthalocyanine derivatives of Renzoni et al are not “hybrid phthalocyanine derivatives” as instantly defined; however, they possess a high degree of structural similarity to those claimed.



14. Thus the rejections under 35 USC 112 and 103 are maintained for reasons of record and the further reasons set forth above.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 8:30 to 6:00.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie E. Garcia, Ph.D.  
July 22, 2001